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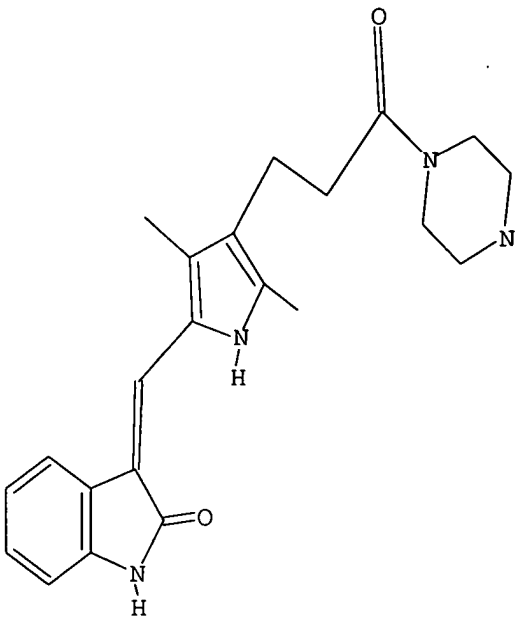
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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FULL SCREEN SEARCH COMPLETED - 1506 TO ITERATE

100.0% PROCESSED 1506 ITERATIONS 19 ANSWERS
SEARCH TIME: 00.00.01

L2 19 SEA SSS FUL L1

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FULL SUBSET SCREEN SEARCH COMPLETED - 19 TO ITERATE

100.0% PROCESSED 19 ITERATIONS 16 ANSWERS
SEARCH TIME: 00.00.01

L5 16 SEA SUB=L2 SSS FUL L3

file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 206.56 207.40

FILE 'CAPLUS' ENTERED AT 11:10:17 ON 04 FEB 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 4 Feb 2005 VOL 142 ISS 6
FILE LAST UPDATED: 2 Feb 2005 (20050202/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l5
L6 5 L5

=> d l6 1-5 ibib abs hitstr

L6 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:143270 CAPLUS
DOCUMENT NUMBER: 140:197593
TITLE: PDGFRα oncokinase fusion protein associated with hyperproliferative disease and as imatinib mesylate target in EOL-1 cell
INVENTOR(S): Briesewitz, Roger; Griffin, John H.
PATENT ASSIGNEE(S): Theravance, Inc., USA
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004015082	A2	20040219	WO 2003-US24992	20030808
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004045044	A1	20040304	US 2003-637356	20030808
PRIORITY APPLN. INFO.:			US 2002-402330P P	20020809
			US 2003-440491P P	20030116

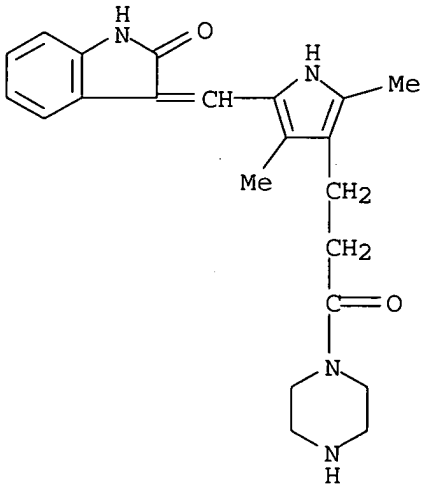
AB Oncokinase fusion protein associated with hyperproliferative disorders are provided. The fusion polypeptides have a C-terminal tyrosine kinase domain fused to an N-terminal domain that is not normally fused to the

C-terminal tyrosine kinase domain and they possess constitutively activated tyrosine kinase activity. The invention provides sequence of protein NM_030917 fused with platelet-derived growth factor receptor α from human. The invention also identified deletion of 1 megabase fuses NM_030917 and exon 12 of PDGFRα on human chromosome 4. Also provided are methods of diagnosing disease conditions associated with the fusion polypeptides. In addition, screening assays for identifying agents useful for treating disease conditions associated with such fusion polypeptides and polynucleotides are provided. Furthermore, methods of treating disease conditions associated with the presence of the fusion polypeptides are provided.

IT **560071-94-5**, THRX-165724
RL: BSU (Biological study, unclassified); BIOL (Biological study) (reducing activity of fusion protein by; PDGFRα oncokinase fusion protein associated with hyperproliferative disease and as imatinib mesylate target in EOL-1 cell)

RN 560071-94-5 CAPLUS

CN Piperazine, 1-[3-[5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-pyrrol-3-yl]-1-oxopropyl]- (9CI) (CA INDEX NAME)



L6 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:551511 CAPLUS
DOCUMENT NUMBER: 139:101028
TITLE: Preparation of pyrrolylmethyleneindolones as protein kinase inhibitors and antitumor agents
INVENTOR(S): Griffin, John H.; Briesewitz, Roger; Wray, Jonathan W.
PATENT ASSIGNEE(S): Theravance, Inc., USA
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003057690	A1	20030717	WO 2002-US41252	20021220

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,

same

UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003171378	A1	20030911	US 2002-327385		20021220
US 6686362	B2	20040203			
EP 1458713	A1	20040922	EP 2002-796035		20021220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
BR 2002015360	A	20041214	BR 2002-15360		20021220
US 2004198804	A1	20041007	US 2003-691094		20031022
PRIORITY APPLN. INFO.:			US 2001-343746P	P	20011227
			US 2001-343813P	P	20011227
			US 2002-327385	A3	20021220
			WO 2002-US41252	W	20021220

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [wherein R1 = H, alkyl; R2 = -A1-NR5R6; R5, R6 = independently H, alkyl; A1 = (CH2)m, (CH2)n-A2-(CH2)p, (CH2CH2O)qCH2CH2; m = 2-10; n, p = 1-6; A2 = CH=CH, phenylene, biphenylene, cyclohexylene, piperazinylene; q = 1-3; or NR1R2 = morpholinyl, (un)substituted azirinyl, azetidinyl, pyrrolidinyl, piperidinyl, azepinyl, azacrown ethers, etc.; R3, R4 = H, halo, alkyl, alkoxy, un(substituted) Ph, SO2NH2 or alkyl/aryl derivs., certain acylamino; and their pharmaceutically acceptable salts] were prepared as receptor tyrosine kinase inhibitors useful in the treatment of proliferative disorders, such as cancer. For example, compound II•(F3CCO2H)x was prepared from 3,5-dimethyl-2,4-pyrrole dicarboxylic acid di-Et ester in 11 steps via condensation with malonic acid, condensation with oxindole, amidation with mono-Boc piperazine and Boc deprotection using TFA. I exhibit an IC50 values of < 10 μM for inhibition of Flt-3, VEGFR and PDGFR tyrosinase kinases. II inhibited mutant Flt-3 tyrosinase kinase with EC50 = 0.24 μM.

IT **560071-95-6P**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrrolylmethylenedihydroindolones as protein kinase inhibitors and antitumor agents)

RN 560071-95-6 CAPLUS

CN Piperazine, 1-[3-[5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-pyrrol-3-yl]-1-oxopropyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

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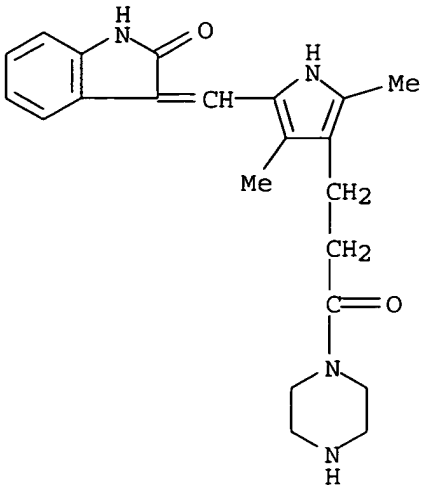
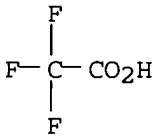
CRN 560071-94-5
CMF C22 H26 N4 O2



CM 2

CRN 76-05-1
CMF C2 H F3 O2



IT **560072-55-1P**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tyrosine kinase inhibitor; preparation of pyrrolylmethylenedihydroindolones as protein kinase inhibitors and antitumor agents)
RN 560072-55-1 CAPLUS
CN Piperazine, 1-[3-[5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-pyrrol-3-yl]-1-oxopropyl]-4-ethyl-, trifluoroacetate (9CI) (CA INDEX NAME)

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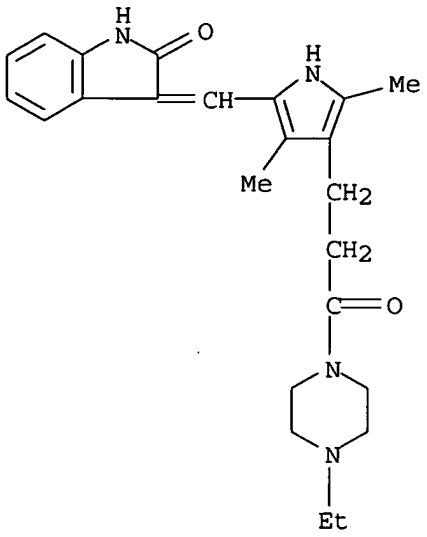
CRN 560072-54-0
CMF C24 H30 N4 O2



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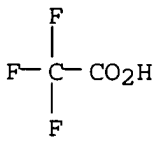
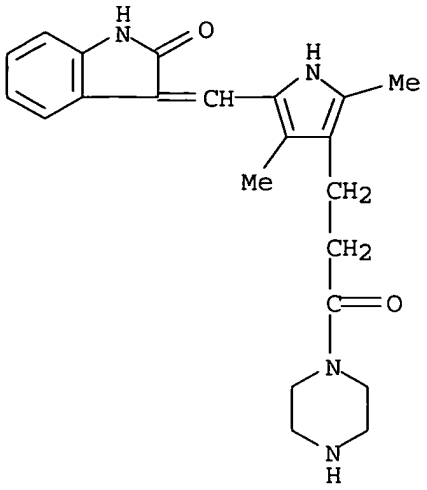
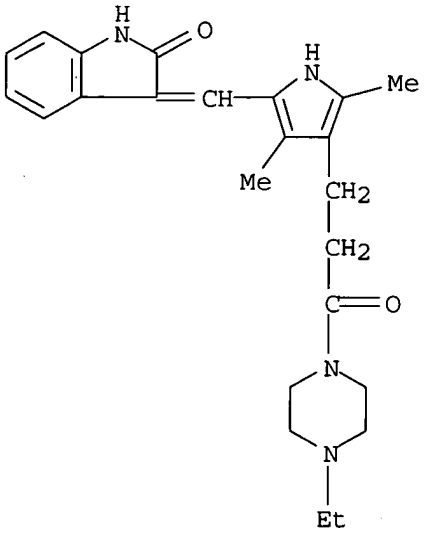
CRN 76-05-1
CMF C2 H F3 O2



IT **560071-94-5P**, 3-[3,5-Dimethyl-4-(3-oxo-3-piperazin-1-ylpropyl)-1H-pyrrol-2-ylmethylene]-1,3-dihydroindol-2-one
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tyrosine kinase inhibitor; preparation of pyrrolylmethylenedihydroindolones as protein kinase inhibitors and antitumor agents)
RN 560071-94-5 CAPLUS
CN Piperazine, 1-[3-[5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-pyrrol-3-yl]-1-oxopropyl]- (9CI) (CA INDEX NAME)



IT **560072-54-0P**, 3-[3,5-Dimethyl-4-[3-oxo-3-(4-ethyl)piperazin-1-ylpropyl]-1H-pyrrol-2-ylmethylene]-1,3-dihydroindol-2-one
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tyrosine kinase inhibitor; preparation of pyrrolylmethylenedihydroindolones as protein kinase inhibitors and antitumor agents)
RN 560072-54-0 CAPLUS
CN Piperazine, 1-[3-[5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-pyrrol-3-yl]-1-oxopropyl]-4-ethyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

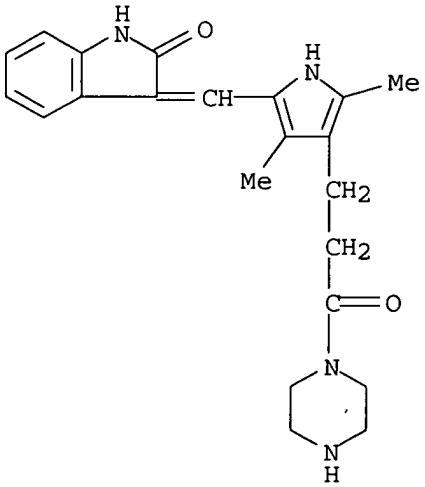
L6 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:521932 CAPLUS
DOCUMENT NUMBER: 139:147708
TITLE: Discovery of a fusion kinase in EOL-1 cells and idiopathic hypereosinophilic syndrome
AUTHOR(S): Griffin, John H.; Leung, Joey; Bruner, Rebecca J.; Caligiuri, Michael A.; Briesewitz, Roger
CORPORATE SOURCE: Theravance, Inc., South San Francisco, CA, 94080, USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2003), 100(13), 7830-7835
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Idiopathic hypereosinophilic syndrome (HES) is a myeloproliferative disease of unknown etiol. Recently, it has been reported that imatinib mesylate (Gleevec), an inhibitor of Bcr-Abl kinase useful in the treatment of chronic myeloid leukemia, is also effective in treating HES; however, the mol. target of imatinib in HES is unknown. This report identifies a genetic rearrangement in the eosinophilic cell line EOL-1 that results in the expression of a fusion protein comprising an N-terminal region encoded by a gene of unknown function with the GenBank accession number NM_030917 and a C-terminal region derived from the intracellular domain of the platelet-derived growth factor receptor α (PDGFRα). The fusion gene was also detected in blood cells from two patients with HES. The authors propose naming NM 030917 Rhe for Rearranged in hypereosinophilia. Rhe-PDGFRα fusions result from an apparent interstitial deletion that links Rhe to exon 12 of PDGFRα on chromosome 4q12. The fusion kinase Rhe-PDGFRα is constitutively phosphorylated and supports IL-3-independent growth when expressed in BaF3 cells. Proliferation and viability of EOL-1 and BaF3 cells expressing Rhe-PDGFRα are ablated by the PDGFRα inhibitors imatinib, vatalanib, and THRX-165724.

IT **560071-94-5P**, THRX 165724
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(discovery of fusion kinase in EOL-1 cells and idiopathic hypereosinophilic syndrome in relation to proliferation/viability ablation by)

RN 560071-94-5 CAPLUS
CN Piperazine, 1-[3-[5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-pyrrol-3-yl]-1-oxopropyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:927188 CAPLUS
DOCUMENT NUMBER: 138:14005
TITLE: Preparation of 5-aralkylsulfonyl-3-(pyrrol-2-

ylmethylidene)-2-indolinone derivatives as kinase inhibitors

INVENTOR(S): Cui, Jingrong; Ramphal, Yudhi; Liang, Congxin; Sun, Li; Wei, Chung Chen; Tang, Peng Cho

PATENT ASSIGNEE(S): USA

SOURCE: PCT Int. Appl., 479 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002096361	A2	20021205	WO 2002-US16841	20020530
WO 2002096361	A3	20030313		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003125370	A1	20030703	US 2002-157007	20020530
US 6599902	B2	20030729		

PRIORITY APPLN. INFO.: US 2001-294544P P 20010530
US 2001-328408P P 20011010

OTHER SOURCE(S): MARPAT 138:14005

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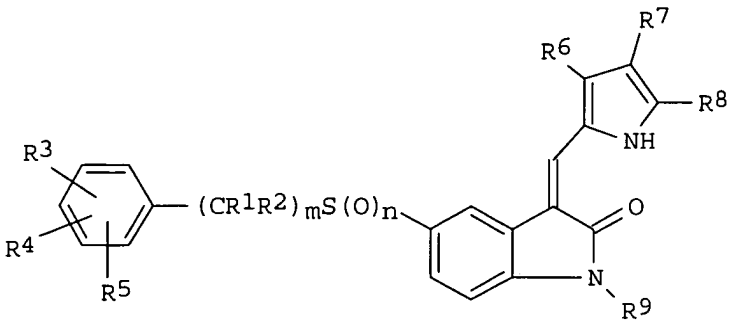


I

AB The present invention relates to certain 5-aralkylsulfonyl-3-(pyrrol-2-ylmethylidene)-2-indolinone derivs. (shown as I; see below for variable definitions; e.g. 2,4-dimethyl-5-(2-oxo-5-phenylmethanesulfonyl-1,2-dihydroindol-(3Z)-ylidenemethyl)-1H-pyrrole-3-carboxylic acid (2-diethylaminoethyl)amide) that inhibit kinases (no data), in particular met kinase. Pharmaceutical compns. comprising these compds., methods of treating diseases mediated by kinases using pharmaceutical compns. comprising these compds., and methods of preparing them are also disclosed. In I: n = 0-2; m = 1-3; R1 and R2 = H or alkyl; R3, R4, and R5 = H, halo, alkyl, cycloalkyl, haloalkyl, hydroxy, alkoxy, alkoxycarbonyl, haloalkoxy, cyano, carboxy, carboxyalkyl, nitro, aryl, aryloxy, heteroaryl, heteroaryloxy, -(alkylene)-CONR10R11, -CONR10R11, or - NR10R11 (R10 is H or alkyl, and R11 is aryl, heteroaryl, heterocycle, aminoalkyl,

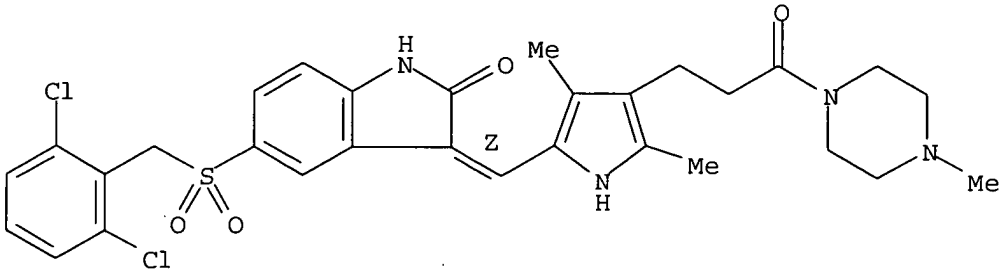
alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, acetylalkyl, cyanoalkyl, carboxyalkyl, alkoxycarbonylalkyl, heteroaralkyl, aralkyl, or heterocyclylalkyl wherein the alkyl chain in aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, aralkyl, heteroaralkyl, or heterocyclylalkyl is optionally substituted with one or two hydroxy, or R10 and R11 together with the N atom to which they are attached combine to form saturated or unsatd. heterocycloamino). R6 is H, alkyl, cycloalkyl, hydroxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, carboxyalkyl, heterocyclylalkyl, aryl, heteroaryl, carboxy, alkoxycarbonyl, heterocyclylcarbonyl, aminoalkylcarbonyl, alkylaminoalkylcarbonyl, dialkylaminoalkylcarbonyl, -CONR10R11 or -(alkylene)-CONR10R11. R7 and R8 = H, alkyl, cycloalkyl, heterocyclylalkyl, -COR12, -(alkylene)-COR12 (R12 = alkoxy, hydroxy, or heterocycle, alkylamino, dialkylamino), -SO2R14, -CONR13R14, or -(alkylene)-CONR13R14 (R13 is H or alkyl, and R14 is aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, acetylalkyl, cyanoalkyl, carboxyalkyl, alkoxycarbonylalkyl, heteroaralkyl, or heterocyclylalkyl wherein the alkyl chain in aminoalkyl, heteroaralkyl, heteroaralkyl, or heterocyclylalkyl is optionally substituted with one or two hydroxy group(s), or when R13 and R14 are attached to a N atom R13 and R14 together with the N atom to which they are attached form saturated or unsatd. heterocycloamino). R6 and R7 or R7 and R8 can combine to form a saturated or unsatd. 5 to 8 membered ring; and R9 is: H or alkyl; -PO(OR15)2 where each R15 = H or alkyl; -COR16 where R16 is H or alkyl; or -CHR17NR18R19 where R17 is H or alkyl, and R18 and R19 = H or alkyl or R18 and R19 together with the N atom to which they are attached form heterocycloamino. Although the methods of preparation are not claimed, 375 example prepns. of I plus addnl. prepns. of intermediates are included.

IT **477577-36-9P**, 5-(2,6-Dichlorophenylmethanesulfonyl)-3-[1-[3,5-dimethyl-4-[3-(4-methylpiperazin-1-yl)-3-oxopropyl]-1H-pyrrol-2-yl]meth-(Z)-ylidene]-1,3-dihydroindol-2-one **477577-37-0P**, 5-(2,6-Dichlorophenylmethanesulfonyl)-3-[1-[4-[3-((3R,5S)-3,5-dimethylpiperazin-1-yl)-3-oxopropyl]-3,5-dimethyl-1H-pyrrol-2-yl]meth-(Z)-ylidene]-1,3-dihydroindol-2-one
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of aralkylsulfonyl- and pyrrolylmethylidene-substituted indolinones as kinase inhibitors useful against cancers and other disorders)

RN 477577-36-9 CAPLUS

CN Piperazine, 1-[3-[5-[(Z)-[5-[[(2,6-dichlorophenyl)methyl]sulfonyl]-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-1H-pyrrol-3-yl]-1-oxopropyl]-4-methyl- (9CI) (CA INDEX NAME)

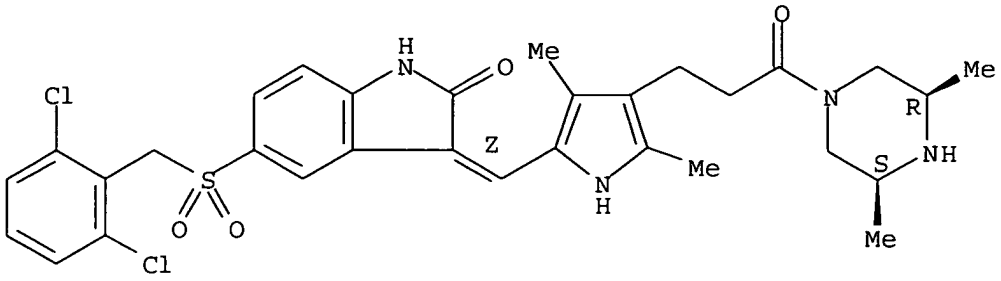
Double bond geometry as shown.



RN 477577-37-0 CAPLUS

CN Piperazine, 1-[3-[5-[(Z)-[5-[[(2,6-dichlorophenyl)methyl]sulfonyl]-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-1H-pyrrol-3-yl]-1-oxopropyl]-3,5-dimethyl-, (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L6 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:539677 CAPLUS
DOCUMENT NUMBER: 137:109202
TITLE: Preparation of 4-aryl substituted indolinones as protein kinase signal transduction modulators for inhibiting abnormal cell proliferation
INVENTOR(S): Cui, Jingrong; Zhang, Ruofei; Shen, Hong; Chu, Ji Yu; Zhang, Fang-Jie; Koenig, Marcel; Do, Steven Huy; Li, Xiaoyuan; Wei, Chung Chen; Tang, Peng Cho
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 560 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002055517	A2	20020718	WO 2001-US48564	20011220
WO 2002055517	A3	20020926		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2432114	AA	20020718	CA 2001-2432114	20011220
US 2003069297	A1	20030410	US 2001-23488	20011220
US 6677368	B2	20040113		
EP 1349852	A2	20031008	EP 2001-997065	20011220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004518669	T2	20040624	JP 2002-556186	20011220
US 2004157909	A1	20040812	US 2003-736243	20031216

PRIORITY APPLN. INFO.:

US 2000-256479P	P	20001220
US 2001-23488	A3	20011220
WO 2001-US48564	W	20011220

OTHER SOURCE(S): MARPAT 137:109202
GI

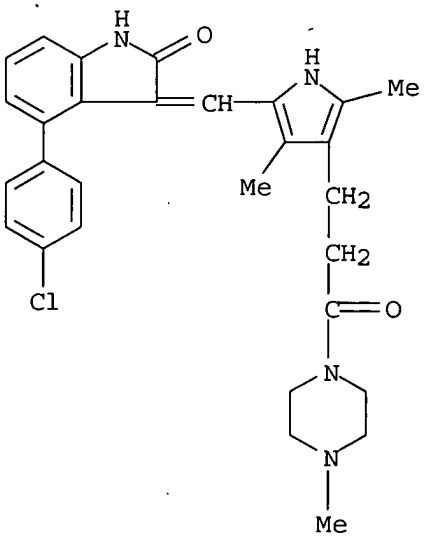
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1 = (un)substituted aryl or heteroaryl; R2 = H, halo, alkyl, alkenyl, alkynyl, heterocyclyl, etc.; R3 = (un)substituted pyrrole or cycloalkenylpyrrole], as well as pharmaceutical compns. thereof, are prepared and disclosed as compds. capable of modulating protein kinase signal transduction in order to regulate, modulate and/or inhibit abnormal cell proliferation. Thus II, was prepared via condensation of 4-phenyl-1,3-dihydroindol-2-one with 5-formyl-2-methyl-4-[3-(4-methylpiperazin-1-yl)propyl]-1H-pyrrole-3-carboxylic acid Et ester. I were evaluated against eight specfic kinases, e.g., FGFR1, for which I possessed IC50 values (μM) of 0.0091-2.07. The present invention also relates to methods for treating protein kinase related disorders.

IT **442559-24-2P 442559-76-4P 442559-77-5P**
442559-78-6P 442560-55-6P 442560-56-7P
442562-39-2P 442562-40-5P 442562-57-4P
442562-58-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of (aryl)(pyrrolylmethylene)indolinones as protein kinase signal transduction modulators)

RN 442559-24-2 CAPLUS

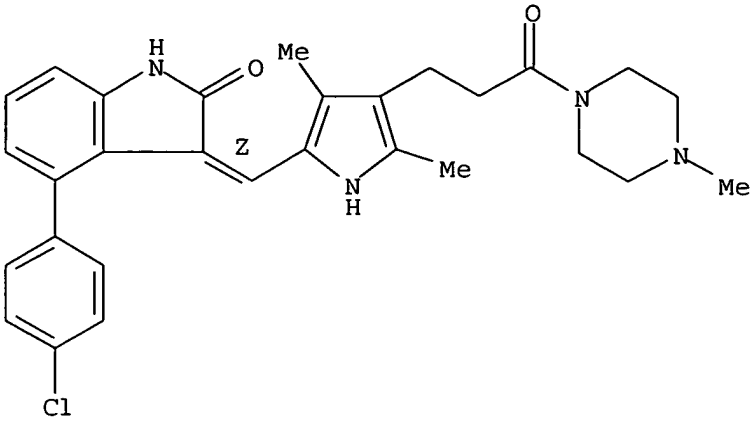
CN Piperazine, 1-[3-[5-[[4-(4-chlorophenyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-1H-pyrrol-3-yl]-1-oxopropyl]-4-methyl- (9CI) (CA INDEX NAME)



RN 442559-76-4 CAPLUS

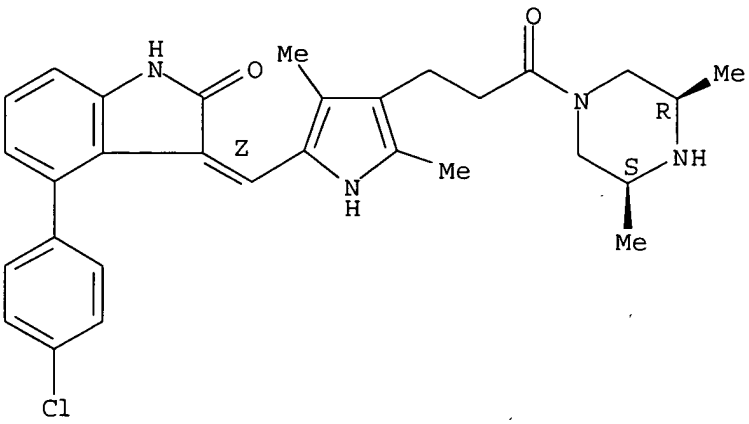
CN Piperazine, 1-[3-[5-[(Z)-[4-(4-chlorophenyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-1H-pyrrol-3-yl]-1-oxopropyl]-4-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 442559-77-5 CAPLUS
CN Piperazine, 1-[3-[5-[(Z)-[4-(4-chlorophenyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-1H-pyrrol-3-yl]-1-oxopropyl]-3,5-dimethyl-, (3R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



RN 442559-78-6 CAPLUS
CN Piperazine, 1-[3-[5-[(Z)-[4-(4-fluorophenyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-1H-pyrrol-3-yl]-1-oxopropyl]-4-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

```
=> E GRIFFIN JOHN H/AU 25
E1            1     GRIFFIN JOHN FRANCIS THOMAS/AU
E2            1     GRIFFIN JOHN G/AU
E3          337 --> GRIFFIN JOHN H/AU
E4            1     GRIFFIN JOHN HAMPTON/AU
E5           35     GRIFFIN JOHN J/AU
E6            5     GRIFFIN JOHN L/AU
E7            3     GRIFFIN JOHN M/AU
E8            1     GRIFFIN JOHN M M/AU
E9            1     GRIFFIN JOHN MARVIN/AU
E10           1     GRIFFIN JOHN MICHAEL/AU
E11          18     GRIFFIN JOHN P/AU
E12           3     GRIFFIN JOHN PATRICK/AU
E13           1     GRIFFIN JOHN PETER/AU
E14           9     GRIFFIN JOHN R/AU
E15           3     GRIFFIN JOHN R JR/AU
E16           6     GRIFFIN JOHN ROBERT/AU
E17           1     GRIFFIN JOHN S/AU
E18           1     GRIFFIN JOHN V/AU
E19          86     GRIFFIN JOHN W/AU
E20           2     GRIFFIN JONATHAN/AU
E21           4     GRIFFIN JONATHAN L W/AU
E22           3     GRIFFIN JONATHAN LUKE WILLIAM/AU
E23           1     GRIFFIN JOSEPH/AU
E24           2     GRIFFIN JOSEPH C/AU
E25           1     GRIFFIN JOSEPH C III/AU

=> S (E3 OR E4) AND (TYROSINE)
            337 "GRIFFIN JOHN H"/AU
              1 "GRIFFIN JOHN HAMPTON"/AU
         138623 TYROSINE
           2437 TYROSINES
         139113 TYROSINE
                  (TYROSINE OR TYROSINES)
L7           12 ("GRIFFIN JOHN H"/AU OR "GRIFFIN JOHN HAMPTON"/AU) AND (TYROSINE)

=> s l7 and proliferative
          36222 PROLIFERATIVE
              7 PROLIFERATIVES
          36225 PROLIFERATIVE
                  (PROLIFERATIVE OR PROLIFERATIVES)
L8            2 L7 AND PROLIFERATIVE

=> s l7 and prolif?
         211190 PROLIF?
L9            2 L7 AND PROLIF?

=> d l9 1-2 ibib abs hitstr

L9   ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2004:143270  CAPLUS
DOCUMENT NUMBER:          140:197593
TITLE:                    PDGFRα oncokinase fusion protein associated with
                          hyperproliferative disease and as imatinib mesylate
                          target in EOL-1 cell
INVENTOR(S):              Briesewitz, Roger; Griffin, John H.
PATENT ASSIGNEE(S):       Theravance, Inc., USA
SOURCE:                   PCT Int. Appl., 95 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
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PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004015082	A2	20040219	WO 2003-US24992	20030808
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004045044	A1	20040304	US 2003-637356	20030808
PRIORITY APPLN. INFO.:			US 2002-402330P	P 20020809
			US 2003-440491P	P 20030116

AB Oncokinase fusion protein associated with hyperproliferative disorders are provided. The fusion polypeptides have a C-terminal **tyrosine** kinase domain fused to an N-terminal domain that is not normally fused to the C-terminal **tyrosine** kinase domain and they possess constitutively activated **tyrosine** kinase activity. The invention provides sequence of protein NM_030917 fused with platelet-derived growth factor receptor α from human. The invention also identified deletion of 1 megabase fuses NM_030917 and exon 12 of PDGFRα on human chromosome 4. Also provided are methods of diagnosing disease conditions associated with the fusion polypeptides. In addition, screening assays for identifying agents useful for treating disease conditions associated with such fusion polypeptides and polynucleotides are provided. Furthermore, methods of treating disease conditions associated with the presence of the fusion polypeptides are provided.

L9 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2003:551511 CAPLUS
DOCUMENT NUMBER:	139:101028
TITLE:	Preparation of pyrrolylmethyleneindolones as protein kinase inhibitors and antitumor agents
INVENTOR(S):	**Griffin, John H.**; Briesewitz, Roger; Wray, Jonathan W.
PATENT ASSIGNEE(S):	Theravance, Inc., USA
SOURCE:	PCT Int. Appl., 39 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003057690	A1	20030717	WO 2002-US41252	20021220
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003171378	A1	20030911	US 2002-327385	20021220
US 6686362	B2	20040203		

EP 1458713	A1	20040922	EP 2002-796035		20021220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
BR 2002015360	A	20041214	BR 2002-15360		20021220
US 2004198804	A1	20041007	US 2003-691094		20031022
PRIORITY APPLN. INFO.:			US 2001-343746P	P	20011227
			US 2001-343813P	P	20011227
			US 2002-327385	A3	20021220
			WO 2002-US41252	W	20021220

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [wherein R1 = H, alkyl; R2 = -A1-NR5R6; R5, R6 = independently H, alkyl; A1 = (CH2)m, (CH2)n-A2-(CH2)p, (CH2CH2O)qCH2CH2; m = 2-10; n, p = 1-6; A2 = CH=CH, phenylene, biphenylene, cyclohexylene, piperazinylene; q = 1-3; or NR1R2 = morpholinyl, (un)substituted azirinyl, azetidinyl, pyrrolidinyl, piperidinyl, azepinyl, azacrown ethers, etc.; R3, R4 = H, halo, alkyl, alkoxy, un(substituted) Ph, SO2NH2 or alkyl/aryl derivs., certain acylamino; and their pharmaceutically acceptable salts] were prepared as receptor **tyrosine** kinase inhibitors useful in the treatment of **proliferative** disorders, such as cancer. For example, compound II•(F3CCO2H)x was prepared from 3,5-dimethyl-2,4-pyrrole dicarboxylic acid di-Et ester in 11 steps via condensation with malonic acid, condensation with oxindole, amidation with mono-Boc piperazine and Boc deprotection using TFA. I exhibit an IC50 values of < 10 μM for inhibition of Flt-3, VEGFR and PDGFR tyrosinase kinases. II inhibited mutant Flt-3 tyrosinase kinase with EC50 = 0.24 μM.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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